Isolated sphenoid sinusitis complicated by meningitis and multiple cerebral infarctions in a renal transplant recipient

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Introduction

Infection was amongst the most feared complications of renal transplantation in the early era of this technique. Serious infection developed in up to 70% of renal transplant recipients, and a subsequent fatal outcome occurred in as many as between 11 and 40% [1]. Improved surgical techniques, more targeted immunosuppression and prophylactic antimicrobial agent use have led to a dramatic reduction in these rates. Nevertheless, infection remains a leading cause of morbidity and mortality at all stages of the post-transplant period [1]. Infections in this population are often unconventional and opportunistic, and therefore active surveillance for infection remains a cornerstone of management. We report a case in which isolated sphenoid sinusitis in a renal transplant recipient led to multiple complications and an ultimately fatal outcome.

Case

A 48-year-old man with end-stage renal failure secondary to glomerulonephritis received a cadaveric renal transplant in May 2001 after 20 months on peritoneal dialysis. Serum creatinine fell to 120 μmol/l 1 week post-transplant with tacrolimus and prednisolone immunosuppression. One episode of biopsy-confirmed rejection at 6 weeks was satisfactorily treated with intravenous methylprednisolone and prednisolone immunosuppression. One episode of biopsy-confirmed rejection at 6 weeks was satisfactorily treated with tacrolimus toxicity, with a rise in serum creatinine to 270 μmol/l. Fever developed, and a further renal biopsy showed CMV inclusion bodies. After confirmation with fluorescence testing and polymerase chain reaction, treatment with intravenous ganciclovir was commenced. Five days later, the patient developed an incapacitating left hemicranial headache. He had a past history of migraine, causing a similar headache. Clinical examination, including neurological, otorhinolaryngological and ophthalmological examinations were unremarkable, apart from mild photophobia without neck stiffness. CT scan and MRI scans showed numerous small foci of abnormal signal in the deep white matter of both cerebral hemispheres, consistent with ischaemic changes; no other abnormality was noted. The headache initially responded to simple analgesia. CMV antigenaemia tests were negative after 2 weeks of intravenous antiviral therapy, and 1 month of oral ganciclovir was substituted. The left hemicranial headache recurred at this time without response to propanolol, rizatriptan and amitriptyline. A further CT scan showed appearances consistent with a small lacunar infarct in the right basal ganglia, but no other abnormality was identified. A lumbar puncture, which had been refused by the patient on earlier occasions, was also performed. The cerebrospinal fluid (CSF) was clear and colourless and analysis was normal apart from a CSF protein of 840 mg/l. Enrichment culture grew coagulase-negative staphylococci and Bacillus sp. which were felt to represent contamination. Tests for herpes simplex virus and CMV in the CSF were negative. A diagnosis of migraine was still considered most likely, and sumatriptan and sodium valproate were introduced.

During weeks 19 and 20, gradual, but marked, systemic deterioration occurred. During this time, repeated thorough clinical evaluation proved unrewarding; the only positive findings being ongoing headache of unaltered character, low mood, lethargy, mild drowsiness and photophobia. Multiple analgesic agents of all major classes were used in combination, with no relief from the headache. Poor oral intake of...
Isolated sphenoid sinusitis is an uncommon disease, which is often associated with many sinister complications. The sphenoid sinus is located deep at the apex of the nasal cavity, and this location results in a paucity of specific symptoms and signs. Up to 98% of patients with inflammatory causes for isolated sphenoid sinusitis have headache on initial evaluation, which is typically non-localizing, and refractory to medical therapy [2]. Other reported initial features are visual loss and cranial nerve defects, each in 12% of cases. Specifically, eye-lid ptosis due to involvement of the third nerve is reported to occur in <1% of patients with inflammatory isolated sphenoid sinusitis [2]. The location of the sinus also places it in close proximity with the cavernous sinus, the optic canal, the pituitary gland and the dura mater. The walls of the sinus can be extremely thin, and bone may be absent [3]. Consequently, barriers to extension of inflammation from the sphenoid sinus into the intracranial cavity are poor. Delay in diagnosis of the condition, which frequently occurs, further facilitates intracranial complications.
We report the first case of complicated isolated sphenoid sinusitis in a renal transplant recipient. Specific risk factors for sphenoid sinus disease have not been identified [2], and this may reflect the small number of cases reported in the literature. Nevertheless, the incidence of infectious episodes in the post-transplant period is related to the net immunosuppressive effect achieved [4]. In our case, the summation of standard post-transplant immunosuppression, allograft rejection and subsequent high doses of corticosteroids [1], CMV infection [3], and deteriorating nutritional status will have produced profound overall immunosuppression, and will have increased the likelihood of fungal infection, manifest in this case as chronic invasive fungal sinusitis, in particular.

Meningitis is the most common complication of sphenoid sinusitis [5], and in one series was present in all patients who succumbed to the disease [6]. However, CSF findings are often misleading, with the CSF white cell count not indicative of the severity of the condition [5], the glucose level frequently normal, and culture of the CSF negative in 60% of cases [6]. Occlusion of the carotid and basilar arteries in association with sphenoid sinus disease has been reported [7,8]. High local concentrations of inflammatory mediators leading to local arterial thrombosis [7], abscess extension to involve the clivus and the basilar artery [8], and adherence of *Aspergillus* hyphae to the inside of major intracerebral arteries [9] are all postulated mechanisms of vascular occlusion in these circumstances.

Our patient had symptoms compatible with sinusitis for 7 weeks, and yet CT scan, MRI scan and CSF examination revealed no evidence of sinusitis, or intracranial extension thereof, during that time. Endoscopic examination was only performed after radiological confirmation of sphenoid sinusitis and associated complications, and no microbiological results were available pre-mortem. A variety of diagnostic tools should be utilized early, and if necessary repeatedly, if isolated sphenoid sinus disease is suspected. Repeated thorough history taking and examination should be employed. CT scan is considered to be the gold standard in the diagnosis of sinusitis [5]. Scans should be performed with and without contrast, including axial and coronal high resolution thin cuts of the sinuses, and should include evaluation of the brain and orbits if intracranial complications are suspected. In patients with meningitis, contrast-enhanced MRI will identify lesions that are not identified by CT scan. MRI studies should consist of non-enhanced T1-weighted and T2-weighted examinations [5]. Endoscopic sphenoid sinus visualization, and appropriate tissue sampling for histology and microbiology, yielded positive findings in 90% of critically ill patients in whom sinusitis was suspected, and frequently led to an alteration in management [10].

The frequent and devastating nature of the complications of sinusitis, and in particular of isolated sphenoid sinusitis, should lead clinicians to seek this diagnosis aggressively in renal transplant recipients with intractable headache or elusive infection.

**Conflict of interest statement.** None declared.

**References**


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